THE QUININ TREATMENT OF RABIES*

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The announcement by Moon[1] of the quinin treatment as a possible cure for rabies attracted much attention. His experiments, though few in number, were seemingly convincing. Shortly after Moon's announcement Harris[2] reported a case of successful cure by the administration of quinin in the human being. Since the report by Harris this treatment has been resorted to without success in at least three cases of hydrophobia in the human subject. As there were insufficient laboratory experiments on the quinin treatment for hydrophobia, and as this treatment was an almost universal failure when tried on human subjects, the following experiments are reported.

It was found that the dose of quinin tolerated by a full-grown rabbit was approximately 1 grain. Larger doses repeated daily were usually fatal, and even the 1-grain dose daily was fatal in several cases. For guinea-pigs the daily dose was 0.5 grain.

The quinin treatment was tested against not only the fixed virus, but also against street virus. The former was a six-day virus, while the latter killed rabbits in about ten days, and guinea-pigs in eight days. The virus was given intracranially; the bisulphate of quinin was used in all experiments, the injections being intraperitoneal.

In Experiment 1, five animals were injected intracranially with varying but small doses of fixed virus. The day following the inoculation three of the animals were injected intraperitoneally with 1 grain of quinin bisulphate. These injections were continued daily until death from rabies resulted. Animals 4 and5 served as controls. Animal 3 died 15 minutes after the first injection of quinin. The symptoms preceding death were typical of quinin poisoning: rapid respiration, marked muscular tremor, unsteady gait, loss of equilibrium, convulsive seizure, and death usually within 45 minutes after injection. All the animals with the exception of Animal 3 died with the usual symptoms of rabies.

In Experiment 2, Animal 1 received no quinin until symptoms of rabies appeared, but the treatment had no appreciable effect. Animal 2 died of quinin poisoning 35 minutes after the second injection. Animal 3, treated with quinin, died from rabies.

Experiment 3 was a duplicate of Experiment 2. Animal 1, however, died from an acute bacillary infection and the quinin treatment had no preventive effect in Rabbits 2 and 3.

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1. *Jour. Infect. Dis.*, 1913, 13, p. 165.
2. *Jour. Am. Med. Assn.*, 1913, 61, p. 1511.

EXPERIMENT 1

Rabbit	Dose Fixed Virus Oct. 14	Quinin Treatment							
		Oct 15	Oct. 16	Oct. 17	Oct. 18	Oct. 19	Oct. 20	Oct. 21	Oct. 22
1	1.05 M.I.D.*	1 grain	1 grain	1 grain	1 grain	1 grain P. P.	1 grain C. P.	+	.....
2	1.2 "	1 grain	1 grain	1 grain	1 grain	1 grain	1 grain	+	.....
3	1.3 "	D	.....	.....	.....	.....	.....	.....	.....
4	1.05 "	.....	.....	.....	.....	.....	C. P.	+	.....
5	1.2 "	.....	.....	.....	.....	P. P.	C. P.	C. P.	+

* Throughout the paper the following abbreviations are used: M.I.D. = the smallest infecting dose of rabic virus; P. P. = partial paralysis in rabies; C. P. = complete paralysis in rabies; D. = death from quinin poisoning; + = death from rabies.

EXPERIMENT 2

Guinea-Pig	Dose Fixed Virus Oct. 13	Quinin Treatment							
		Oct. 28	Oct. 29	Oct. 30	Oct. 31	Nov. 1	Nov. 2	Nov. 3	Nov. 4
1	1.0 M.I.D.	.....	..... D	.....	.....	.....	P. P. 1 grain	C. P. 1 grain	+
2	1.05 "	1 grain	1 grain	.....	.....	.....	..... C. P.	.....	.....
3	1.25 "	1 grain	1 grain	1 grain	1 grain	1 grain	1 grain	+	.....

EXPERIMENT 3

Rabbit	Dose Fixed Virus Oct. 27	Quinin Treatment							
		Oct. 28	Oct. 29	Oct. 30	Oct. 31	Nov. 1	Nov. 2	Nov. 3	Nov. 4
1	1.0 M.I.D.	.....	+*	.....	.....	.....	..... P. P.	..... C. P.	.....
2	1.05 "	1 grain	1 grain	1 grain	1 grain	1 grain	1 grain C. P.	1 grain C. P.	+
3	1.25 "	1 grain	1 grain	1 grain	1 grain	1 grain	1 grain	1 grain	+

* Not rabies.

EXPERIMENT 4

Rabbit	Fixed Virus Subcutaneously Oct. 27	Quinin Treatment	Nov. 18	Dec. 15
1	2500 M.I.D.	Daily injections (1 grain) until death	+	..
2	" "	.....	..	+

In Experiment 4 the fixed virus was given subcutaneously. Although the dose given is equal to 2,500 M. I. D. by the intracranial route, it is not always an infecting dose when given subcutaneously. Animal 1 was treated daily with 1 grain of quinin during the incubation period of 21 days; Animal 2 served as control. Both animals died from rabies.

Beginning October 28, two rabbits received eight daily injections of 1 grain of quinin without any untoward symptoms. On the ninth day each was injected with a small dose of rabic virus. The injections of ½ grain of quinin were continued daily until death from rabies, on November 13, the treatment having had no appreciable effect. A similar experiment with guinea-pigs gave a like result. In this case the preliminary treatment extended over three days.

EXPERIMENT 5

Rabbit	Street Virus Nov. 12	Quinin Treatment	Nov. 23	Nov. 24	Nov. 27	Nov. 28
1	0.5 c.c.	Daily injections of 1 grain	.....	P. P.	C. P.	+
2	0.5 c.c.	Daily injections of 1 grain	.....	.....	.....	.....
Guinea-Pig						
1	0.5 c.c.	Daily injections of 0.5 grain	P. P.	+	.....	.....
2	0.5 c.c.	Daily injections of 0.5 grain	+	.....	.....	.....

The animals in Experiment 8 were injected intracranially with street virus and received during the incubation period daily injections of quinin. Rabbit 2 apparently did not become infected. Insusceptibility, though rare, does occur in animals injected even with fixed virus. The other three animals in this experiment died from rabies.

SUMMARY

The experiments were controlled both as to the infectivity of the virus and as to the absence, for the most part, of untoward symptoms from the quinin treatment.

The dose of virus in most of the tests was not much larger than the smallest infecting dose. This amount of the virus is approximately one-two-hundred-thousandth (1/200,000) part of the total virus in the brain and spinal cord of a rabbit at the beginning of the paralytic stage. In the case of hydrophobia in man we have no exact data as to the amount of virus, but it probably is many times greater than in the rabbit. Assuming that there is a quantitative reaction between the quinin and the virus, the protection — if any — afforded by large doses of quinin against a small infecting dose of virus should be easily demonstrated experimentally. Inasmuch as the quinin failed as a preventive measure against extremely small doses of virus in actual tests, can it not reasonably be assumed that this method of treatment is of no curative value in cases of hydrophobia manifesting symptoms

in which the amount of virus would be many thousand times greater? In the absence of protection by quinin against small doses of virus, even when a series of daily injections of quinin is given preliminary to the injection of rabic virus, we cannot expect favorable results from quinin after symptoms of hydrophobia have developed.